tion and is excreted. Persistence of a high G : N ratio does not, however, necessarily indicate even a maximal breakdown of body tissue. Thus two cases may each show equally high G : N ratios, but the one individual may excrete much less glucose and nitrogen than the other. In this case the prognosis would obviously be more favorable, other factors being equal. The duration of the disease, the degree of hyperglycemia, effect of ingestion of carbohydrates on the blood sugar and the glycosuria, the severity of other clinical symptoms, and the nature of previous treatment must also be carefully considered in judging of the prognostic value of this ratio in any particular instance. This is well exemplified by the very interesting case of Geyelin and Du Bois, in which a suddenly developing complete diabetes with high G : N ratio rapidly subsided under judicious treatment. This patient also illustrates the important fact that a high G : N ratio is not without exception an indication of a fatal termination of the disease.

In several instances recently studied the G : N ratio has slightly exceeded the value 3.4 : 1. In such subjects it is probable that carbohydrate already present in the body plays a role. The excretion of this carbohydrate as glucose during the fasting periods is the very probable cause of the G : N ratios of these cases being higher than 3.4 : 1, which has been shown by our work to represent in complete diabetes the average value of this quotient for urine. It is very probable that had the fasting days in these cases having G : N ratios over 3.4 : 1 been sufficiently numerous this lower ratio would have been observed.

SUMMARY. By means of improved experimental methods it could be established that the fasting urinary G : N ratio of severe diabetes mellitus is about 3.4 : 1. The G : N ratio is, therefore, to be regarded as a definite index of the severity of this disease. In association with other factors to be considered, the G : N ratio is a valuable prognostic sign.

OBSERVATIONS ON THE STARVATION TREATMENT OF DIABETES.

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AND

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FOR the past year we have been treating all cases of diabetes admitted to the Royal Victoria Hospital, on the starvation plan.

Those patients who remained under the strict supervision, and those who, when away, made an intelligent effort to carry out the treatment, did well, and have remained sugar-free on the prescribed diet, proved after varying periods to be suited to their tolerance.

Difficulties, however, arose with those unwilling, or unable, to follow the directions, and these difficulties, needless to say, were numerous. No doubt the supreme difficulty will always be that either the patient, or the doctor, fails to appreciate the need of strict attention to the treatment. So much precision in the diet is necessary, for severe cases, that even in the hospital routine, it has often been extremely difficult to carry out a successful treatment except with full coöperation of the patient.

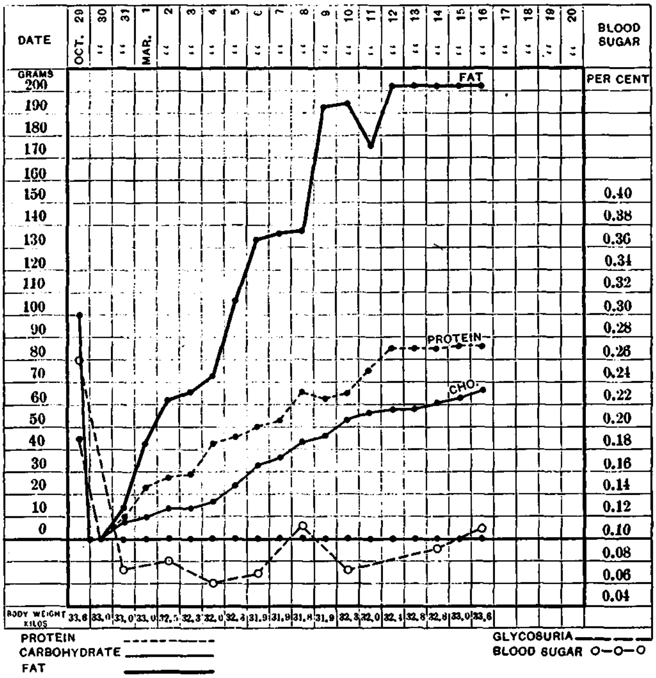


CHART I.

Again, our knowledge of the exact values of foodstuffs is still insufficient, more especially that branch relating to appreciation of the values of cooked and uncooked foods, notably the carbohydrates, and the proteins with their CHO content.

That there is greater need of standardization in our dietetic treatment is more and more apparent, and without an attempt to make clear the values of foods given, it is difficult for observers to fully coöperate in work of this nature.

The simple example may be cited of CHO values in various vegetables; while some observers compute in their estimate of CHO food administered only the available CHO, others again include the total amount, of which unused cellulose forms a considerable portion, and alters entirely the value of our given foods. So, too, in boiled vegetables, while some compute the water in which CHO are boiled, others discard it, even though a not inconsiderable amount of available food in it should be estimated if we are to aim at exactness in our computations.

On the other hand, it is a matter of occasional surprise that patients can sometimes disregard these dietetic prescriptions with impunity. Particularly noteworthy is an instance of a patient with moderately severe diabetes, upon whom, after successful starvation treatment had conferred benefit, periodical alcoholic bouts and late nights of dissipation seemed to have no deleterious effects.

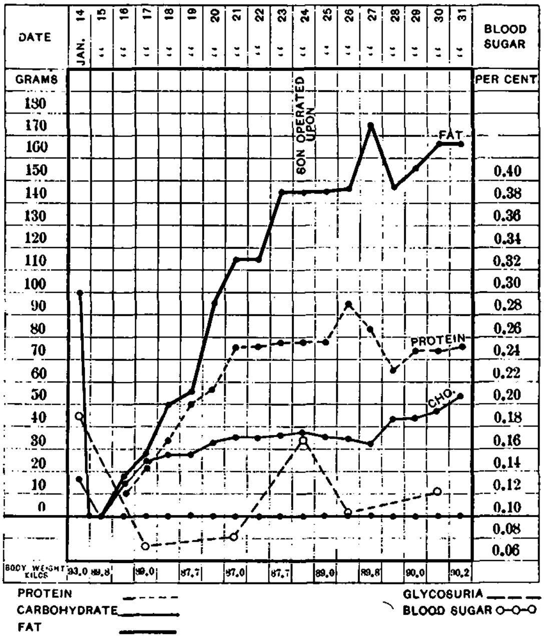


Chart II.

In two of our cases, however, fatigue and nervousness seemed to markedly aggravate an already existing glycosuria, this view coinciding with those recently emphasized by Cannon (see Chart II).

In one much-worried patient, with a glycosuria of 12 per cent., rest and relief from anxiety alone were followed by a reduction to 2 per cent. on the following day.

As a rule, one or two days of starvation sufficed to render the urine sugar-free, and in only one instance was the period as long as five days.

In the moderately severe cases it was found that patients could be raised to a tolerance of high caloric value in amazingly short time (See Chart I), but it has not seemed possible in raising the CHO tolerance to avoid the return of a hyperglycemia. In fact, in our limited experience it would seem that the metabolic disturbance which is implied by the term diabetes is not eradicated by any dietetic treatment, but merely subdued during the period of absolute precise treatment.

During the starvation treatment it was not found necessary, except in one instance, to use alcohol during the early days of treatment. In one case (Chart I), all forms of foodstuffs were raised to a very high level of value and maintained with excellent results while the patient was under supervision; but, as a rule, it was found that the more gradual and slow attaining of tolerance seemed the wiser plan, and when accompanied by a weekly starvation day the level of tolerance was raised with much greater success.

In the satisfactory cases the striking features were the speed at which sufficient satisfying food could be given, and the patient maintained upon a low level of food supply with an absence of hunger, thirst, fatigue, or loss of weight, and a general feeling of well-being seemed to exist when the proper level was maintained.

During the early treatment the loss of weight seemed rarely to be marked—in one case over 20 pounds, and in two others 13 pounds—while in the rest the loss of weight never exceeded 5 pounds. Later on the normal weight was either recovered or remained but little below the original level. Perhaps insufficient attention has been drawn to this fact, and the impression is too wide-spread that the starvation treatment is one of reduction, with severe emaciation, whereas in reality the subjective and objective evidences of starvation are not present.

Examination of Blood-sugar. The blood-sugar was periodically examined in every case. After the patient's admission an estimate was first formed of the approximate severity of the disease, together with the percentage of blood-sugar and then 100 grams of glucose were given on the first day of starvation, and the blood-sugar thereafter determined every hour for four hours.

Experience in the case of three or four patients, however, revealed the fact that four hours was an insufficient period in which properly to estimate the blood-sugar curves. We have recently extended these observations to cover twelve to twenty-four hours, and discovered thereupon that the hyperglycemia is more persistent than had been supposed.

The results by comparison with normal individuals were of great interest:

Experimental Glucose Curve of Normal Individuals. In the normal person there is, of course, an increase of blood-sugar after 100 grams of glucose have been administered, but the curve occupies a much lower level, usually dropping below the normal in two or three hours. The maximum is attained at the end of the first hour, becomes normal again at the second hour, goes below the normal at the end of the third hour, and finally rises again to normal in four to five hours (see Chart III).

The normal threshold we regard as 0.14 per cent.

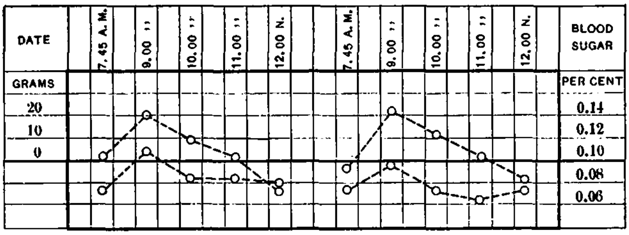


Chart III.

Experimental Glucose Curve of Diabetics. In diabetes, however, the curve was markedly altered and prolonged, as was found in repeated observations, in which, of course, we kept all individuals under exactly uniform conditions.

One hour after administration of the glucose the percentage rose, attaining its maximum at the end of the second hour, rarely at the end of the third.

The decline followed, but at a rate much slower than in normal individuals. The implication is that in diabetes, the liver not being able to hold the sugar in amount and duration as in the normal, causes a higher percentage of blood-sugar to appear.

The excursion is greater, the ascent more acute, the maximum appearing sometimes rapidly, sometimes more slowly, the variations, however, not depending on severity. As a rule, the maximum was reached at the end of two hours, and the decline was slow, occupying often eight to twelve hours (see Chart IV).

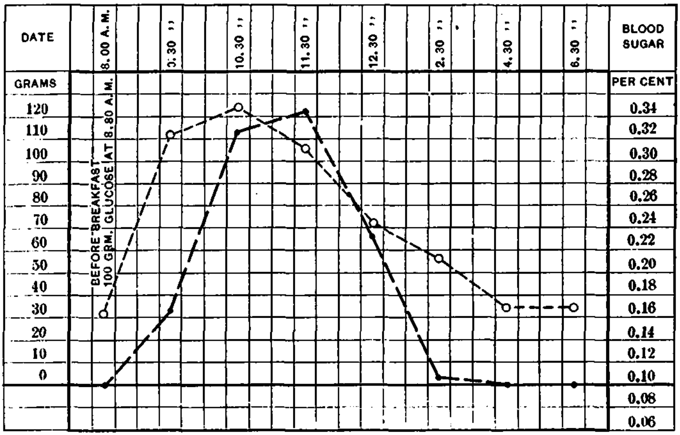
These observations seem to confirm those of Falta, who emphasized their importance in diabetes.

The abnormally slow decline in the blood-sugar curve in the later hours of the test on diabetics, possibly suggests some kind of kidney-block, and varies according to the rate of excretion, and in part, too, of course, to the degree of combustion.

Renal Block. This question of kidney-block is apparently an unsolved problem, but the more careful and repeated examinations for blood-sugar have demonstrated its importance as well as the intimate relation in many cases between glycosuria and renal function. It was found that with starvation the disappearance of the glycosuria has usually preceded the subsidence of hyperglycemia. However, our experience in one respect is at variance with Joslin, who states that during starvation the hyperglycemia persisted, while in the majority of our cases it disappeared rapidly with starvation.[1]

With gradual increase in the diet, however, the blood-sugar rose to an abnormal degree, usually in the absence of glycosuria.

Various factors seem to play a part in inducing block, and the causes are difficult to explain; in three of our cases the values ran as high as 0.22 per cent. 0.26 per cent. and 0.28 per cent. without glycosuria. In other cases with glycosuria of long duration the block appeared, though at a lower level.



TOTAL GLYCOSURIA=33.45 GRM.

Chart IV.

A certain prognostic importance is attached to renal block in diabetes, for it would seem that the degree of hyperglycemia varies directly with the tendency to progression and the development of complications.

An insidious and progressive diabetes may often be overlooked when glycosuria is absent, and when an appreciation of the block may yield a more intelligent means of dealing with the patient.

Evidently sufficient stress is not laid upon the hour at which these estimates are made. Thus, for example, the hyperglycemia came on at first about two hours after meals, at which time we think the estimates should always be made as giving us the best guide to the diabetic changes. Blood-sugars in the majority of our diabetics were found to be normal in the early morning before breakfast, while two hours after meals a hyperglycemia was evident, this depending, of course, in part upon the diet. Often, however, when the diet was restricted in accordance with the treatment the same experience occurred.

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[1] Arch. Int. Med., vol. xvi, p. 703.

The following figures will indicate the differences: Before breakfast: 0.11 per cent., 0.10 per cent., 0.18 per cent. After breakfast: 0.15 per cent., 0.16 per cent., 0.24 per cent.

Renal Glycosuria and Block. In one of our patients, persistent glycosuria appeared whenever the blood-sugar rose to a level of 0.11 per cent.; at no time was there much glycosuria, and he always reacted to starvation; 27 grams of carbohydrate per day would induce a glycosuria which was not increased with an intake up to 50 grams.

Before meals his blood-sugar was 0.08 to 0.09 per cent., while after a mixed meal his blood-sugar rose to 0.11, or 0.12 per cent. with slightly glycosuria (see Chart V).

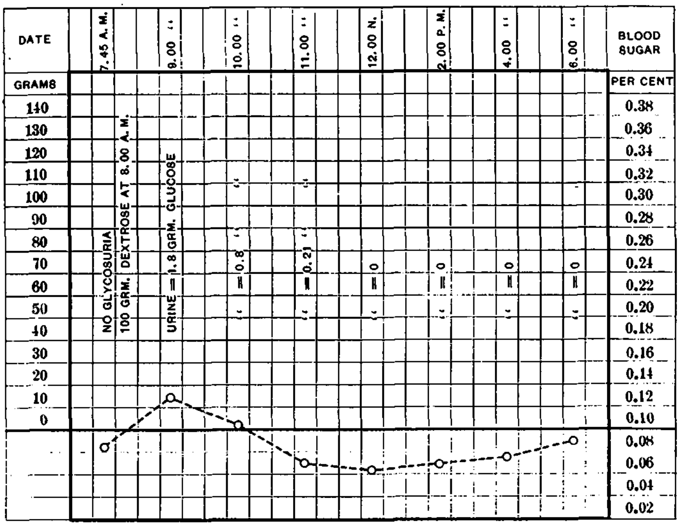

Chart V.

As a result of recent work, no doubt, the more frequent estimations of blood-sugar will demonstrate that renal diabetes so-called is less rare than has hitherto been believed.

Test Diet. In some cases a patient's tolerance seems to alter in a very short time, and appreciation of this is of the greatest importance in the use of test diets. Thus, for example, in one individual who had had a fat protein diet for three days, preceded by a low CHO intake for one week, there was a D : N ratio of 2.77 per cent., showing an inability to burn 43 per cent. of protein carbohydrates. He continued on a fat protein diet for twenty-one days, and during the first fourteen days the D : N ratio varied markedly, finally dropping to zero on the sixteenth day. On this day he burned 36 grams of protein CHO as well as 2 grams of CHO in 100 grams of chicken (*i. e.*, 38 grams CHO).

Reading the variations according to the Lusk-Falta formula we found the following:

$$\frac{35.9 \times 100}{12.97 \times 3.65 + 0} = 75.6 \qquad 13 \text{ days later, } \frac{3.08 \times 100}{9.32 \times 3.65 + 2} = 8.5$$

Acidosis. Two important points are worthy of note in our observations:

1. The ferric chloride reaction is sometimes absent when acidosis is present, and is less sensitive, too, than the nitro-prusside reaction. 2. The urine does not always show a reaction for acidosis even when the blood gives a positive quantitative result. This latter is important as reminding us that the excretion of the acid bodies is not necessarily an index of the degree of acidosis.

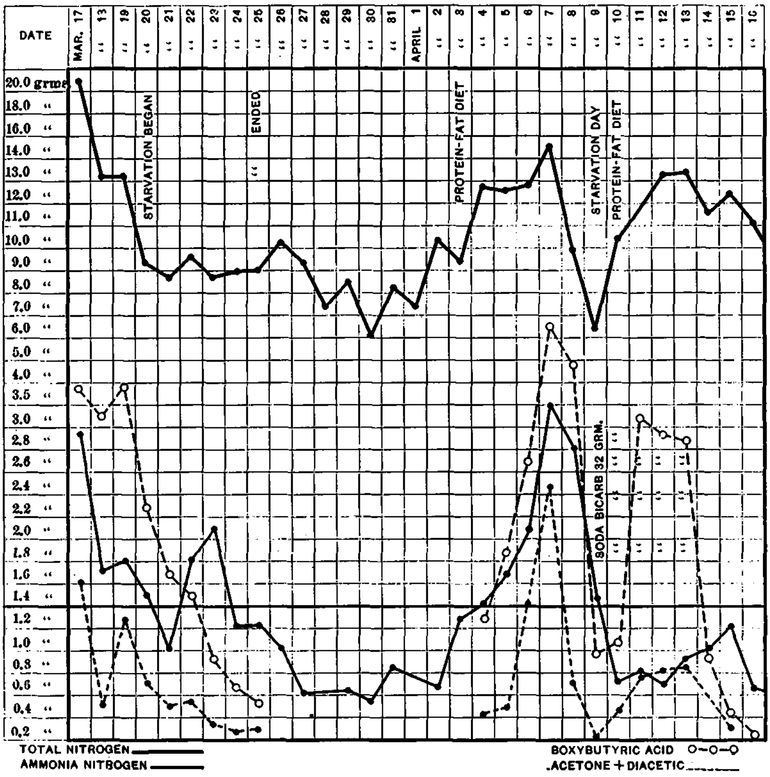

Chart VI.

Starvation in the ordinary individual usually results in acidosis, while in diabetes the reverse occurs. Allen, indeed, lays stress on this feature, and insists on the need of eliminating ketone bodies from the blood by means of starvation.

Sometimes, however, in our cases, acidosis was initiated by the starvation, at other times a preëxisting acidosis was increased, though usually it disappeared. Evidently there is a variation due to many circumstances, though starvation ultimately does make the urine acid-free.

In one persistent case of very mild diabetes, with prolonged mild acidosis, interrupted periods of a fat-free diet seemed especially useful in clearing up remnants of the acidosis.

In one very severe case in which the acidosis disappeared on starvation, it developed again on a protein fat diet, and later on disappeared with one day of starvation. Sodium bicarbonate was given (32 grams per diem) for five days, with resulting elimination of more ketone bodies. Excretion of these bodies ceased again with cessation of bicarbonate administration (see Chart VI).

Another experience worthy of note is the varying ratio of the acetone bodies to β-oxybutyric acid. Sometimes there is much acetone and little β-oxybutyric acid, and sometimes the reverse occurs. There seems to be little constancy, and the percentage of 60 to 80, as usually recorded is subject to many wide exceptions.

THE INFLUENCE OF ACIDOSIS ON HYPERGLYCEMIA IN DIABETES MELLITUS.

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and

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Total fasting or the prolonged withdrawal of carbohydrates from the dietary of a normal or diabetic individual leads to the production of an acidosis. This is usually explained on the following grounds: (1) fats are oxidized secondarily through the combustion of carbohydrates:[2] (2) because of the withdrawal of carbohydrates (and also with the limitation of proteins) more fat than usual is called upon to supply the body energy. The resulting increased mobilization of fats associated with their incomplete combustion leads to the production of acid bodies. An increased protein metabolism (occurring synchronously) may add to or augment the production of similar substances.

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[1] Work done under the tenure of the Moses Heineman Fellowship in Pathology.

[2] Naunyn: Der Diabetes Mellitus, 1906, p. 221.